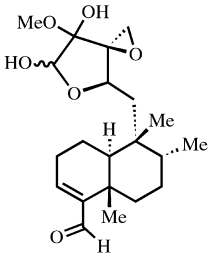
*Bioorg. Med. Chem. 9 (2001) 1365*

## Investigation of the Biological Mode of Action of Clerocidin Using Whole Cell Assays

Colin Jamora,[a] Maria A. Theodoraki,[b] Vivek Malhotra[a] and Emmanuel A Theodorakis[b]

[a]*Department of Biology, University of California San Diego, 9500 Gilman Drive, La Jolla, CA 92093, USA*
[b]*Department of Chemistry and Biochemistry, University of California San Diego, 9500 Gilman Drive No. 0358, La Jolla, CA 92093-0358, USA*

The effect of clerocidin on the growth of HeLa cells was examined. Our results suggest that this compound binds to topoisomerase II prior to formation of cleavable complex with DNA and exhibits its lethal action by inducing cell cycle arrest at the G2/M phase, ultimately leading to apoptosis. Furthermore, clerocidin was found not to affect transcription, translation and the secretory ability of cells until the onset of apoptosis, attesting to the specific antimitotic profile of this drug.




clerocidin

*Bioorg. Med. Chem. 9 (2001) 1371*

## Signaling Pathways and Effector Mechanisms Pre-Programmed Cell Death

Neal B. Blatt[a] and Gary D. Glick[a,b]

[a]*Department of Chemistry, University of Michigan, Ann Arbor, MI 48109-1055, USA*
[b]*Department of Biological Chemistry, University of Michigan, Ann Arbor, MI 48109-1055, USA*

Apoptosis, or pre-programmed cell death, is a complex biochemical process that involves all aspects of the cell from the plasma membrane to the nucleus. Apoptosis stimuli are mediated by many different cellular processes including protein synthesis and degradation, the alteration in protein phosphorylation states, the activation of second messenger systems, and disruption of normal mitochondrial function. Despite this diversity in signal transduction, all apoptotic pathways are believed to converge ultimately with the activation of caspases leading to the characteristic morphological changes of apoptosis. In this review, we discuss what is known about these pathways and its implication for normal cellular function.

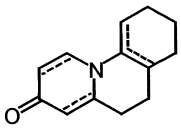
*Bioorg. Med. Chem. 9 (2001) 1385*

## Effect of C-ring Modifications in Benzo[*c*]quinolizin-3-ones, New Selective Inhibitors of Human 5$\alpha$-reductase 1

Antonio Guarna,[a] Ernesto G. Occhiato,[a] Fabrizio Machetti,[a] Andrea Trabocchi,[a] Dina Scarpi,[a] Giovanna Danza,[b] Rosa Mancina,[b] Alessandra Comerci[b] and Mario Serio[b]

[a]*Dipartimento di Chimica Organica 'U. Schiff' and Centro di Studio sulla Chimica e la Struttura dei Composti Eterociclici e loro Applicazioni, C.N.R., Università di Firenze, Via G. Capponi 9, I-50121 Firenze, Italy*
[b]*Dipartimento di Fisiopatologia Clinica, Unità di Endocrinologia, Università di Firenze, Viale Pieraccini 6, I-50134 Firenze, Italy*

Non-steroidal octahydro- and decahydrobenzo[*c*]quinolizin-3-one inhibitors displayed an interesting selectivity toward human enzyme 5α-reductase type 1, the most potent having $IC_{50} = 58$ nM.



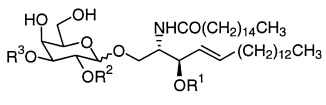

*Bioorg. Med. Chem. 9 (2001) 1395*

## Novel Mimics of Sialyl Lewis X: Design, Synthesis and Biological Activity of a Series of 2- and 3-Malonate Substituted Galactoconjugates

Anne Marinier,[a] Alain Martel,[a] Carol Bachand,[a] Serge Plamondon,[a] Brigitte Turmel,[a] Jean-Paul Daris,[a] Jacques Banville,[a] Philippe Lapointe,[a] Carl Ouellet,[a] Pierre Dextraze,[a] Marcel Menard,[a] John J. K. Wright,[b] Julie Alford,[c] Debbie Lee,[c] Paul Stanley,[c] Xina Nair,[c] Gordon Todderud[c] and Kenneth M. Tramposch[c]

[a]*Department of Chemistry, Bristol-Myers Squibb Pharmaceutical Research Institute, 100, blvd. de l'Industrie, Candiac, Canada J5R 1J1*
[b]*Bristol-Myers Squibb Pharmaceutical Research Institute, Wallingford, CT, USA*
[c]*Dermatological Disease, Bristol-Myers Squibb Pharmaceutical Research Institute, Buffalo, NY, USA*

A series of potent inhibitors of P-selectin as potential antiinflammatory agents is reported. Lead compounds having a greater potency than sialyl Lewis X are identified.



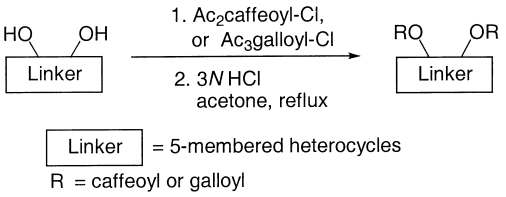

$R^2$ or $R^3 = (CH_2)_nCH(CO_2H)_2$

*Bioorg. Med. Chem. 9 (2001) 1429*

## Dicaffeoyl- or Digalloyl Pyrrolidine and Furan Derivatives as HIV Integrase Inhibitors

Dong Jin Hwang,[a,b] Sun Nam Kim,[a] Jung Hoon Choi[b] and Yong Sup Lee[a]

[a]*Division of Life Sciences, Korea Institute of Science & Technology, PO Box 131, Cheongryang, Seoul 130-650, South Korea*
[b]*Department of Chemistry, Hanyang University, Seoul 133-791, South Korea*



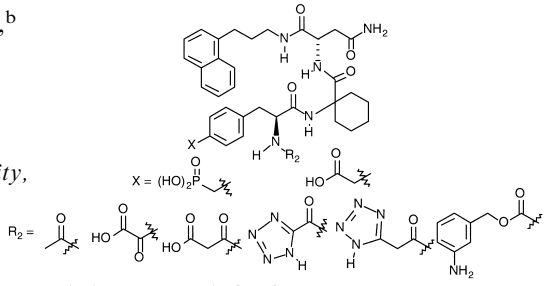

Dicaffeoyl or digalloyl compounds joined through a five-membered heterocyclic ring were synthesized for HIV integrase inhibitors. The inhibitory activities of dicaffeoyl derivaitives were comparable to L-chioric acid ($IC_{50} = 24.9\,\mu M$). On the other hand, digalloyl derivatives were more potent than L-chicoric acid with $IC_{50}$ values of 4.7–15.6 μM.

*Bioorg. Med. Chem. 9 (2001) 1439*

## N-Terminal Carboxyl and Tetrazole-containing Amides as Adjuvants to Grb2 SH2 Domain Ligand Binding

Terrence R. Burke, Jr.,[a] Zhu-Jun Yao,[a] Yang Gao,[a] Jane X. Wu,[b] Xiaofeng Zhu,[b] Juliet H. Luo,[b] Ribo Guo[b] and Dajun Yang[b]

[a]*Laboratory of Medicinal Chemistry, Division of Basic Sciences, National Cancer Institute, National Institutes of Health, Building 376, FCRDC, Frederick, MD 21702-1201, USA*
[b]*Department of Oncology, Lombardi Cancer Center, Georgetown University, Washington, DC 20007, USA*



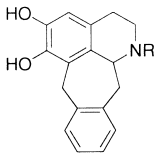

Analogues examined for Grb2 SH2 domain binding potency

*Bioorg. Med. Chem. 9 (2001) 1447*

## Synthesis and Preliminary Pharmacological Evaluation of 5-Hydroxy- and 5,6-Dihydroxy-1,2,3,7,12,12a-hexahydrobenzo[5,6]cyclohepta[1,2,3-*ij*]isoquinoline Derivatives as Dopamine Receptor Ligands

Gian Mario Cingolani,[a] Antonio Di Stefano,[b] Fabrizio Napolitani,[a] Barbara Mosciatti,[a] Gianfabio Giorgioni,[a] Nunzia Cinone,[b] Luigi Brunetti,[b] Grazia Luisi,[b] Barbara Michelotto,[b] Giustino Orlando,[b] Barbara Costa,[c] Antonio Lucacchini,[c] Claudia Martini[c] and Francesco Claudi[a]

[a]*Dipartimento di Scienze Chimiche, Università di Camerino, Via S. Agostino 1, 62032 Camerino (MC), Italy*
[b]*Dipartimento di Scienze del Farmaco, Università "G. D'Annunzio", Via dei Vestini 31, 66100 Chieti, Italy*
[c]*Dipartimento di Psichiatria, Neurobiologia, Farmacologia e Biotecnologie, Università di Pisa, 56126 Pisa, Italy*




A series of 5-hydroxy- and 5,6-dihydroxy-1,2,3,7,12,12a-hexahydrobenzo[5,6]cyclohepta[1,2,3-*ij*]isoquinoline derivatives were synthesized and evaluated for their affinity at $D_1$ and $D_2$ dopamine receptors.

*Bioorg. Med. Chem. 9 (2001) 1459*

## Selenotyrosine and Related Phenylalanine Derivatives

Howard E. Ganther

*Department of Nutritional Science, 1415 Linden Drive, University of Wisconsin-Madison, Madison, Wisconsin 53706, USA*

A new series of Se-substituted phenylalanine derivatives has been synthesized having the para position of the phenyl ring substituted by selenocyanate (-SeCN), seleninic acid (-$SeO_2$ H), or selenol (-SeH) functional groups. The starting material for synthesis was 4′-aminophenylalanine.

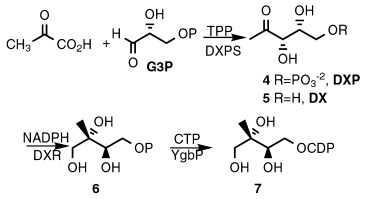
*Bioorg. Med. Chem. 9 (2001) 1467*

## Molecular Cloning, Expression and Characterization of the First Three Genes in the Mevalonate-Independent Isoprenoid Pathway in *Streptomyces Coelicolor*

David E. Cane, Cathy Chow, Antonietta Lillo and Ilgu Kang

*Department of Chemistry, Box H, Brown University, Providence, RI 02912-9108, USA*

The characterization of three enzymes responsible for isoprenoid biosynthesis in *Streptomyces coelicolor* is reported.



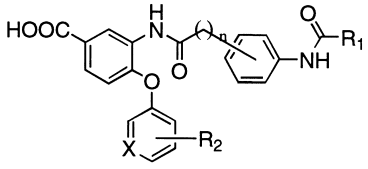

*Bioorg. Med. Chem. 9 (2001) 1479*

## Studies on Selectin Blocker. 9. SARs of Non-Sugar Selectin Blocker against E-, P-, L-Selectin Bindings

Hideki Moriyama, Yasuyuki Hiramatsu, Takao Kiyoi, Toshio Achiha, Yoshimasa Inoue and Hirosato Kondo

*Department of Chemistry, Nippon Organon K.K., R&D Laboratories, 1-5-90 Tomobuchi-Cho, Miyakojima-Ku, Osaka 534-0016, Japan*

As a part of study of selectin blockers, we have investigated SARs of non-sugar selectin antagonists successfully discovered using a computational screening. As a result, computational screening using 3D-pharmacophore model could be useful methodology to find out a new lead for the several type of selectin blockers.



*Bioorg. Med. Chem. 9 (2001) 1493*

## Synthesis and DNA Nicking Studies of a Novel Cyclic Peptide: Cyclo[Lys-Trp-Lys-Ahx-]

Chong-Teh Cheng, Vivian Lo, Johnson Chen, Wan-Chi Chen, Cheng-Yun Lin, He-Ching Lin, Chia-Hung Yang and Leung Sheh

*Department of Chemistry, Tunghai Christian University, Taichung, Taiwan 407 ROC*

A synthetic cyclic peptide: cyclo[Lys-Trp-Lys-Ahx-] was found to have DNA nicking properties on natural supercoiled ϕX174 DNA whereas cyclo[Lys-Tyr-Lys-Ahx-] and Lys-Tyr-Lys did not posses similar activity. The DNA nicking rate increased with increase in temperature. At reaction temperatures lower than 60 °C, the DNA nicking rate of cyclo[Lys-Trp-Lys-Ahx-] exceeded that of linear Lys-Trp-Lys.

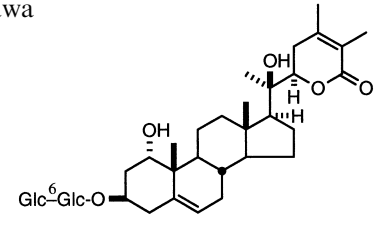
*Bioorg. Med. Chem. 9 (2001) 1499*

## Structures of Withanosides I, II, III, IV, V, VI, and VII, New Withanolide Glycosides, from the Roots of Indian *Withania somnifera* DUNAL. and Inhibitory Activity for Tachyphylaxis to Clonidine in Isolated Guinea-Pig Ileum

Hisashi Matsuda, Toshiyuki Murakami, Akinobu Kishi and Masayuki Yoshikawa

*Kyoto Pharmaceutical University, Misasagi, Yamashina-ku, Kyoto 607-8412, Japan*

Seven new withanolide glycosides called withanosides I, II, III, IV, V, VI, and VII were isolated from an Indian natural medicine, Ashwagandha, the roots of Indian *Withania somnifera* (Solanaceae), together with four known compounds, withaferin A, 5α,20α$_F$(*R*)-dihydroxy-6α,7α-epoxy-1-oxowitha-2,24-dienolide, physagulin D, and coagulin Q. The structures of withanosides I–VII were determined based on chemical and physicochemical evidence. Principal constituents, withanoside VI (10 and 30 μM) and withaferin A (10 μM), attenuated the tachyphylaxis to clonidine on electrically stimulated guinea-pig ileum in vitro.




withanoside VI

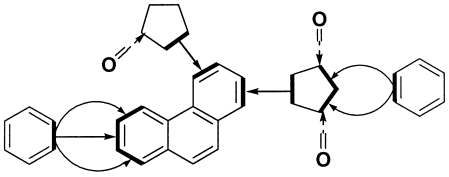
*Bioorg. Med. Chem. 9 (2001) 1509*

## Synthesis and Structure–Mutagenicity Relationship of Benzo-Annulated Cyclopentaphenanthrenes

Assunta Marrocchi,[a] Lucio Minuti,[a] Guido Morozzi[b] and Aldo Taticchi[a]

[a]*Dipartimento di Chimica, Università degli Studi di Perugia, Via Elce di Sotto 8, 06123 Perugia, Italy*
[b]*Dipartimento di Scienze Biochimiche e Biotecnologie Molecolari, Sezione di Scienze Igienistiche e Ambientali, Università degli Studi di Perugia, Perugia, Italy*

The effects of benzoannulation of the carbonyl function on the mutagenicity of several cyclopentaphenanthrenes have been discussed.



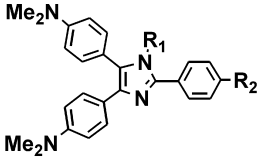
*Bioorg. Med. Chem. 9 (2001) 1517*

## 3D-QSAR Analysis of 2,4,5- and 2,3,4,5-Substituted Imidazoles as Potent and Nontoxic Modulators of P-Glycoprotein Mediated MDR

Ki H. Kim

*Department of Structural Biology, Abbott Laboratories, Abbott Park, IL 60064-6100, USA*

3D-Quantitative structure–activity relationships of 2,4,5- and 2,3,4,5-substituted imidazoles as a novel class of potent and nontoxic modulators of Pgp mediated MDR were investigated using CoMFA and COMSIA approaches.



(**I**)

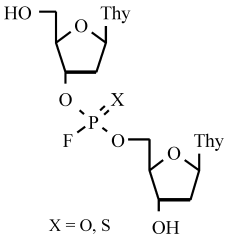
*Bioorg. Med. Chem. 9 (2001) 1525*

## Synthesis, Chemical and Enzymatic Reactivity, and Toxicity of Dithymidylyl-3′,5′-phosphorofluoridate and -phosphorothiofluoridate

Konrad Misiura,[a] Daria Szymanowicz[a] and Halina Kuśnierczyk[b]

[a]*Department of Bioorganic Chemistry, Centre of Molecular and Macromolecular Studies, Polish Academy of Sciences, Sienkiewicza 112, 90-363 Łódź, Poland*
[b]*Department of Tumour Immunology, Institute of Immunology and Experimental Therapy, Polish Academy of Sciences, R. Weigla 12, 53-114 Wrocław, Poland*

Dithymidylyl-3′,5′-phosphorofluoridate and phosphorothiofluoridate are hydrolytically unstable, are not inhibitors of snake venom, spleen phosphodiesterases and alkaline phosphatase, and neither is highly toxic.

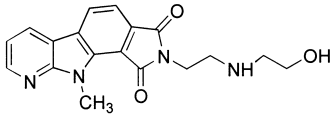


*Bioorg. Med. Chem. 9 (2001) 1533*

## Synthesis, Cytotoxicity, DNA Interaction and Topoisomerase II Inhibition Properties of Tetrahydropyrrolo[3,4-*a*]carbazole-1,3-dione and Tetrahydropyrido-[3,2-*b*]pyrrolo[3,4-*g*]indole-1,3-dione Derivatives

Benoît Joseph,[a] Michaël Facompré,[b] Hervé Da Costa,[a] Sylvain Routier,[a] Jean-Yves Mérour,[a] Pierre Colson,[c] Claude Houssier[c] and Christian Bailly[b]

*Institut de Chimie Organique et Analytique, UMR 6005, Université d'Orléans, BP 6759, 45067 Orléans Cedex 2, France*
[b]*INSERM U-524 et Laboratoire de Pharmacologie Antitumorale du Centre Oscar Lambret, IRCL, Place de Verdun, 59045 Lille, France*
[c]*Laboratoire de Chimie Macromoléculaire et Chimie Physique, Université de Liège au Sart-Tilman 4000 Liège, Belgium*



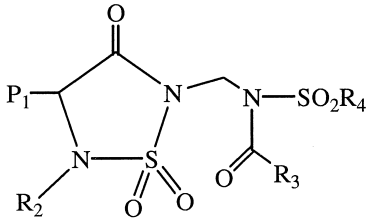
*Bioorg. Med. Chem. 9 (2001) 1543*

## Inhibition of Serine Proteases by Functionalized Sulfonamides Coupled to the 1,2,5-thiadiazolidin-3-one 1,1 Dioxide Scaffold

William C. Groutas, Shu He, Rongze Kuang, Sumei Ruan, Juan Tu and Ho-Kit Chan

*Department of Chemistry, Wichita State University, Wichita, KS 67260, USA*

Potent inhibitors of human leukocyte elastase, proteinase 3 and cathepsin G that interact with the S and S′ subsites are realized by using functional sulfonamides coupled to the 1,2,5-thiadiazolidin-3-one 1,1 dioxide scaffold.



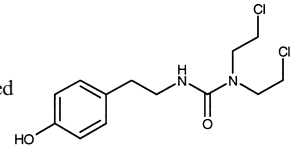
*Bioorg. Med. Chem. 9 (2001) 1549*

## Melanocyte-Directed Enzyme Prodrug Therapy (MDEPT): Development of Second Generation Prodrugs for Targeted Treatment of Malignant Melanoma

Allan M. Jordan,[a] Tariq H. Khan,[b] Hugh Malkin,[a] Helen M.I. Osborn,[a] Andrew Photiou[c] and Patrick A. Riley[d]

[a]*Department of Chemistry, University of Reading, Whiteknights, Reading RG6 6AD, UK*
[b]*Department of Medical Oncology, Imperial College of Science, Technology and Medicine, Charing Cross Campus, London W6 8RP, UK*
[c]*Skin Tumour Unit, St. John's Institute of Dermatology, St. Thomas' Hospital, Lambeth Palace Road, London SE1 7EH, UK*
[d]*Department of Molecular Pathology, Windeyer Institute, UCL Medical School, London W1P 6DB, UK*

Evaluation of second generation prodrugs for MDEPT, by oximetry, has highlighted structural properties that are advantageous and disadvantageous for efficient oxidation using mushroom tyrosinase. In particular, a sterically undemanding prodrug bis-(2-chloroethyl)amino-4-hydroxyphenylaminomethanone was synthesised and found to be oxidised by mushroom tyrosinase at a superior rate to tyrosine methyl ester, the carboxylic acid of which is the natural substrate for tyrosinase.



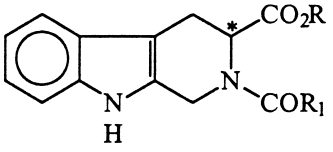
*Bioorg. Med. Chem. 9 (2001) 1559*

## Synthesis, Molecular Modeling and QSAR Studies in Chiral 2,3-disubstituted-1,2,3,4-tetrahydro-9H-pyrido(3,4-b)indoles as Potential Modulators of Opioid Antinociception

Anil K. Saxena,[a] Suresh K. Pandey,[a] Ravish C. Tripathi[a] and Ram Raghubir[b]

[a]*Division of Medicinal Chemistry, Central Drug Research Institute, Lucknow 226001, India*
[b]*Division of Pharmacology, Central Drug Research Institute, Lucknow 226001, India*

Some semi-rigid racemic and chiral analogues of a potent CCK receptor antagonist (benzotript) have been synthesized and tested for their modulatory role on opioid anti-nocicicception mediated by CCK-B. Among these compounds, **3e**, **3g**, **3h**, **4a**, **4b** and **4h**, exhibited antinociceptive potentiation comparable to benzotript and proglumide. The 3D-biophore models depicting three biophoric sites for π/hydrophobic interactions, hydrogen bonding and ionic interactions have been described, where total hydrophobicity and *S*-configuration (C-3) contributes for potentiation of anti-nociception.



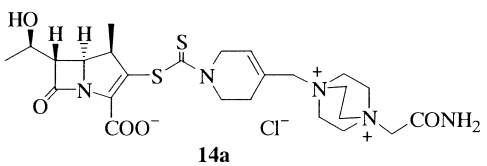
*Bioorg. Med. Chem. 9 (2001) 1571*

## Dicationic Dithiocarbamate Carbapenems with Anti-MRSA Activity

Hideaki Imamura, Norikazu Ohtake, Hideki Jona, Aya Shimizu, Minoru Moriya, Hiroki Sato, Yuichi Sugimoto, Chinatsu Ikeura, Hideo Kiyonaga, Masato Nakano, Rie Nagano, Shinnosuke Abe, Koji Yamada, Terutaka Hashizume and Hajime Morishima

*Banyu Tsukuba Research Institute, Banyu Pharmaceutical Co., Ltd, Okubo-3, Tsukuba 300-2611, Ibaraki, Japan*

A new class of dicationic dithiocarbamate 1β-methylcarbapenems was prepared. Especially, **14a** was showed good anti-MRSA activity in vivo and DHP-I susceptibility.



**14a**

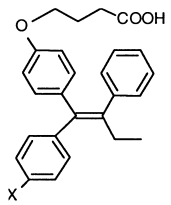
*Bioorg. Med. Chem. 9 (2001) 1579*

## Identification of New Triarylethylene Oxyalkanoic Acid Analogues as Bone Selective Estrogen Mimetics

Valeria N. Rubin, Peter C. Ruenitz, F. Douglas Boudinot and Jason L. Boyd

*College of Pharmacy, University of Georgia, Athens, GA 30602-2352, USA*

Oxybutyric acids **6** and **7** have been found to have an activity profile similar to estabished selective estrogen receptor modulators (SERMs) with significant bone protecting effects and minimal uterotrophic activity




X
OH **6**
H **7**

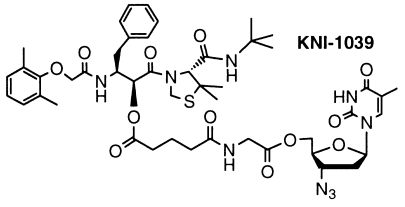
*Bioorg. Med. Chem. 9 (2001) 1589*

## Design, Synthesis, and Biological Evaluation of Anti-HIV Double-Drugs: Conjugates of HIV Protease Inhibitors with a Reverse Transcriptase Inhibitor through Spontaneously Cleavable Linkers

Hikaru Matsumoto,[a] Tooru Kimura,[a] Tomonori Hamawaki,[a] Akira Kumagai,[a] Toshiyuki Goto,[b] Kouichi Sano,[b] Yoshio Hayashi[a] and Yoshiaki Kiso[a]

[a]*Department of Medicinal Chemistry, Center for Frontier Research in Medicinal Science, Kyoto Pharmaceutical University, Yamashina-ku, Kyoto 607-8412, Japan*
[b]*Department of Microbiology, Osaka Medical College, Takatsuki-shi, Osaka 569-8686, Japan*

KNI-1039, a double-drug conjugating an HIV potease inhibitor with AZT by a glutarylglycine linker, exhibited excellent anti-HIV activity.




*Bioorg. Med. Chem. 9 (2001) 1601*

## Synthesis and Antimicrobial Activity of the Symmetric Dimeric Form of Temporin A Based on 3-*N*,*N*-di(3-aminopropyl)amino Propanoic Acid as the Branching Unit

Helena Hujakka,[a] Jari Ratilainen,[b] Timo Korjamo,[a] Hilkka Lankinen,[c] Pentti Kuusela,[d,e] Harri Santa,[a] Reino Laatikainen[a] and Ale Närvänen[a]

[a]*University of Kuopio, Department of Chemistry, PO Box 1627, FIN-70211 Kuopio, Finland*
[b]*Orion Corporation, Orion Pharma, Department of Synthetic Chemistry, PO Box 65, FIN-02101 Espoo, Finland*
[c]*Haartman Institute, Peptide and Protein Laboratory, Department of Virology, PO Box 21, FIN-00014 Helsinki University, Helsinki, Finland*
[d]*Haartman Institute, Department of Bacteriology and Immunology, FIN-00014 Helsinki University, Helsinki, Finland*
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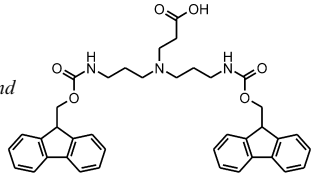
The novel molecule 3-*N*,*N*-di(3-aminopropyl)amino propanoic acid (DAPPA) (**1**) was used as the branching unit in the dimerization of an antimicrobial peptide Temporin A (TA). The dimerization caused a change in the net charge of the TA from +2 to +4. The change in the net charge also altered the antimicrobial activity of the TA leading to improved antibacterial properties especially against Gram-negative bacteria.



**1**

*Bioorg. Med. Chem. 9 (2001) 1609*

## Synthesis and Phosphodiesterase 5 Inhibitory Activity of Novel Phenyl Ring Modified Sildenafil Analogues

Dae-Kee Kim, Namkyu Lee, Ju Young Lee, Do Hyun Ryu, Jae-Sun Kim, Suk-Ho Lee, Jin-Young Choi, Kieyoung Chang, Young-Woo Kim, Guang-Jin Im, Won-Son Choi, Tae-Kon Kim, Je-Ho Ryu, Nam-Ho Kim and Kyoungrim Lee

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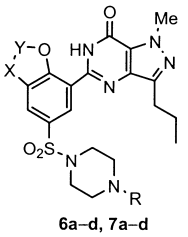
Synthesis, ab initio calculations and in vitro PDE activities of new sildenafil analogues containing an ether ring fused into the phenyl moiety, **6a–d** and **7a–d**, are described.




**6a–d, 7a–d**

**6**: R = Me
**7**: R = $(CH_2)_2OH$
**a**: X, Y = $(CH_2)_2$
**b**: X, Y = $(CH_2)_3$
**c**: X = O, Y = $CH_2$
**d**: X = O, Y = $(CH_2)_2$

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## Synthesis and Properties of Triple Helix-Forming Oligodeoxyribonucleotides Containing 7-Chloro-7-deaza-2′-deoxyguanosine

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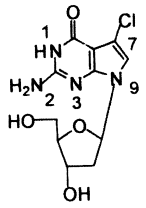
We report multiple incorporations of 7-chloro-7-deaza-2′-deoxyguanosine G* in place of 2′-deoxyguanosine into a triple helix-forming oligodeoxyribonucleotide (TFO) involving a run of six contiguous G. The incorporation of the modified nucleoside slightly increases triplex stability and decreases the TFO auto-association.

G* =




*Bioorg. Med. Chem. 9 (2001) 1625*

## Introduction of the New Dipeptide Isostere *7-Endo*-BtA as Reverse Turn Inducer in a Bowman-Birk Proteinase Inhibitor: Synthesis and Conformational Analysis

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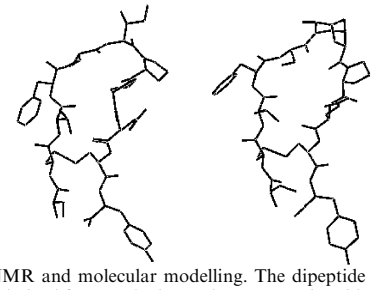

Two dipeptide isosteres 7-*exo*-BTG (**1**) and 7-*endo*-BtA (**2**), belonging to the new *class* of γ/δ-bicyclic amino acid BTAa, were inserted into an 11-residue peptide deriving from the Bowman Birk Inhibitor (BBI) class of serine protease inhibitors, and the conformational properties of these modified peptides have been studied by NMR and molecular modelling. The dipeptide isostere 7-*endo*-BtA [(1*R*,4*S*,5*R*,7*R*)-4-*endo*-methyl-6,8-dioxa-3-azabicyclo[3.2.1]octane-7-*endo*-carboxylic acid] (**2**), derived from L-alanine and *meso* tartaric acid, gave rise to the modified BBI peptide **5** whose structure was very similar to that of the original peptide **3**, suggesting a possible reverse turn inducing property for this dipeptide isostere.

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## Salen Complexes with Bulky Substituents as Useful Tools for Biomimetic Phenol Oxidation Research

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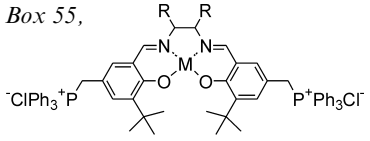
The catalytic effect of bulky water-soluble salen complexes on the oxidation of phenolic lignin model compounds is studied.




M = Co(II), Cu(II), Fe(III), Mn(III)

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## Synthesis and Study of a Cyclic Angiotensin II Antagonist Analogue Reveals the Role of π*–π* Interactions in the C-Terminal Aromatic Residue for Agonist Activity and Its Structure Resemblance with $AT_1$ Non-Peptide Antagonists

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The cyclic analogue along c-[Sar[1], Lys[3], Glu[5]] Ile[8] ANG II **18** has been designed and synthesized in an attempt to reveal the stereoelectronic similarities between its C-terminal region and non-peptide mimetics $AT_1$ antagonists. The rational design of this analogue reveals that π*–π* interactions between the key animoacids Tyr[4]-Phe[8] are critical for agonist activation.